

What is claimed is:

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1. A method of treating cystic fibrosis in a mammal, said method comprising administering to said mammal a first compound in a therapeutically effective amount to enhance the trafficking of a mutant CFTR polypeptide to the surface of an epithelial cell in said mammal, said first compound being administered on a chronic intermittent schedule, thereby preventing  
10 induction of tolerance to said first compound, and administering to said mammal a second compound in a therapeutically effective amount to increase the chloride ion transport activity of said mutant CFTR polypeptide at the surface of said cell, wherein, the  
15 chloride ion transport function of said mutant CFTR polypeptide is enhanced at the surface of said cell, thereby treating said cystic fibrosis in said mammal.

2. The method of claim 1, wherein said mammal is a  
20 human.

3. The method of claim 1, wherein said mutant CFTR polypeptide is  $\Delta F508$ -CFTR.

4. The method of claim 1, wherein said first compound is selected from the group consisting of butyrate, phenylbutyrate, 4-phenylbutyrate, and a biologically active analog of butyrate or phenyl  
25 butyrate.

5. The method of claim 11, wherein said second compound is selected from the group consisting of an isoflavone and a flavone.

6. The method of claim 1, wherein said second  
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compound is genistein or a biologically active analog thereof.

5 7. The method of claim 1, wherein said first compound and said second compound are administered to said mammal together as components of the same composition.

10 8. The method of claim 1, wherein said first compound and said second compound are administered to said mammal as components of different compositions.

15 9. The method of claim 1, wherein said first compound is administered to said mammal prior to administering said second compound to said mammal.

20 10. The method of claim 1, wherein said first compound is administered to said mammal from about 4 hours to about 48 hours prior to administering said second compound to said mammal.

25 11. The method of claim 1, wherein said first compound is administered to said mammal orally.

30 12. The method of claim 1, wherein said second compound is administered to said mammal by a route selected from the group consisting of topically, orally, parenterally, by inhalation and intravenously.

35 13. The method of claim 11, wherein said epithelial cell is selected from the group consisting of a nasal epithelial cell, a lung epithelial cell, a pancreatic epithelial cell, an intestinal epithelial cell, a biliary epithelial cell and a sweat duct epithelial cell.

14. A kit for treating cystic fibrosis in a human patient, said kit comprising

5 a) a first compound in a therapeutically effective amount to enhance the trafficking of a mutant CFTR polypeptide to the surface of an epithelial cell in said human patient;

10 b) a second compound in a therapeutically effective amount to increase the chloride ion transport activity of said mutant CFTR polypeptide; and

15 c) an instructional material which directs the use of a) and b) for the function of treating cystic fibrosis in a human patient and optionally contains instructions for administration of the compounds on an intermittent treatment schedule.

15. The kit of claim 14, further comprising d) a device for providing delivery of one or more of said first compound and said second compound in an aerosolized formulation.

20 16. The method of claim 1; wherein said chronic intermittent treatment schedule comprises administration of said first compound for a duration of one to two weeks followed by a two to four week period wherein said first compound is not administered and said second  
25 compound is administered 2 days following the administration of compound 1.

30 17. The method of claim 1, wherein said chronic intermittent treatment schedule comprises administration of said first compound for a duration of three to four days followed by a two to four week period wherein said first compound is not administered.

